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Dedicated to the 115th anniversary of B.A. Arbuzov's birth

Synthesis of New Phosphorylated 1,2,4-Triazole-3-thiones. N,S-Functionalization Methods

E. L. Gavrilova[a]*, I. A. Krutov[a], A. A. Valieva[a], Kh. R. Khayarov[a,b], A. I. Samigullina[c], A. T. Gubaidullin[c], N. I. Shatalova[a], R. N. Burangulova[a], and O. G. Sinyashin[a,c]

[a] *Kazan National Research Technological University, ul. K. Marksa 68, Kazan, Tatarstan, 420015 Russia*
**e-mail: gavrilova_elena_@mail.ru*

[b] *Kazan (Volga Region) Federal University, ul. Kremlevskaya 18, Kazan, Tatarstan, 420008 Russia*

[c] *A.E. Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center, Russian Academy of Sciences, ul. Akademika Arbuzova 8, Kazan, Tatarstan, 420088 Russia*

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Abstract—New phosphorylated 1,2,4-triazole-3-thiones have been synthesized, and the possibility of their N,S-functionalization has been demonstrated. The direction of alkylation of 1,2,4-triazole-3-thiones with ethyl acrylate has been shown to depend on the substituent on the N^4 atom.

Keywords: 1,2,4-triazole-3-thione, N,S-functionalization, alkylation, phosphorylated 1,2,4-triazole-3-thiones

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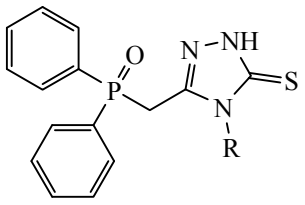
1,2,4-Triazole-3-thiones exhibit a broad spectrum of biological activity [1, 2]; therefore, synthesis of new structures based thereon, in particular of those containing a pharmacophoric phosphoryl group, seems to be promising. There are published data on the synthesis of some phosphorylated bis-1,2,4-triazole-3-thiones [3] in which two 1,2,4-triazole heterocycles are separated by a phosphorus-containing ethylidene or ethylene fragments. However, these are the only known examples of research in the field of phosphorylated triazolethiones.

We previously described the synthesis of new phosphorylated 1,2,4-triazole-3-thiones **1a** and **1b** [4] by heterocyclization of the corresponding phosphorylated thiosemicarbazides based on Fosenazid (diphenylphosphorylacetic acid hydrazide) which is a neurotropic drug [5] (Scheme 1). In continuation of these studies, we have synthesized new phosphorylated 1,2,4-triazole-3-thione **1c** (Scheme 2).

Triazolethione molecules possess two nucleophilic centers, which provides the possibility of their modification at the sulfur or nitrogen atom [6, 7]. The synthesis of ethyl triazolylsulfanylacetates by S-alkylation of triazoles **1a** and **1b** with ethyl bromoacetate and subsequent hydrazinolysis with the goal of obtaining the corresponding hydrazides were described by us in [4]. Herein we report the synthesis of ethyl triazolylsulfanylacetate **3** (the product of alkylation of triazole **1c** with ethyl bromoacetate) and triazolylsulfanylacetohydrazide **4** (Scheme 3).

Triazolethiones can be alkylated with α,β-unsaturated compounds [8, 9] such as ethyl acrylate. It is known that the alkylation of triazolethiones with ethyl acrylate involves the N^2 atom as nucleophilic center [8, 9]. We have found that both nitrogen and sulfur atoms could be nucleophilic centers in the alkylation of

Scheme 1.



1a–**1c**

R = H (**a**), Ph (**b**), All (**c**).